Remarks/Arguments

Claims 1, 3-5, and 46-48 are pending in the application.

First Rejection Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection of claims 1, 3-5 and 46-48 under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner continues to assert that what is enabled by the specification is not commensurate with the scope of the claims. The rejection is improper because the Examiner has not met the initial burden of establishing a reasonable basis for questioning what is provided by the specification.

The Examiner asserts that the specification confines its teachings to administration of a specific anti-EGFR/HER1 antibody (C225) in combination with a chemotherapeutic agent to a cancer patient who suffered from psoriasis. To the contrary, and as the Applicant has previously pointed out, the specification discloses treatment of a hyperproliferative disease (*e.g.*, psoriasis) by sole administration of an EGFR antibody or other EGFR antagonist (e.g., page 3, lines 9-15). The specification also discloses that, in addition to administration of an EGFR antagonist alone, an EGFR antagonist can be administered in combination with any conventional treatment (including, *e.g.*, phototherapy or a chemotherapeutic agent). However, nowhere in the specification is there a suggestion that any agent in addition to an EGFR antagonist is required to practice the invention.

The Examiner argues that a claim directed to treatment of psoriasis with an EGFR antibody is not commensurate with the scope of the specification because the working example describes a treatment in which CPT-11 is co-administered. First, compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. (MPEP § 2164.02). However, the instant specification does indeed provide a working example. In the example, a patient having psoriasis and refractory colon cancer was treated with an EGFR antibody and exhibited a complete response with respect to psoriasis. CPT-11 was included because cancer was the primary disease being treated. Although the Examiner presupposes that CPT-11 is somehow required for the observed

improvement in psoriasis, there is no such suggestion in the specification. The claimed subject matter is commensurate with the disclosure.

The Examiner's position appears to turn on the supposition that CPT-11 must be administered in order for there to be a response. However, while the Examiner has deemed the Applicant's arguments to be unpersuasive, the Patent Office still has not met its burden of providing a reasonable basis for its position that the pending claims are not enabled. Nor has the Examiner provided any rationale for the belief that administration of CPT-11 would have any use for treatment of psoriasis. To establish a reasonable basis, the Examiner must provide a reasonable explanation as to why the scope of protection of a claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). In the instant application, where the specification discloses the claimed invention, it is incumbent on the Patent Office to explain why it doubts the truth or accuracy of the supporting disclosure and to back up its assertions with its own evidence or reasoning as to inaccuracy of the disclosure. (*In re Marzocchi*, 439 F.2d 200, 224, 169 USPQ 367, 370 (CCPA 1971). At best, the Office's position that claims are not enabled if they do not recite co-administration of CPT-11 is mere supposition. Thus, the Applicant asserts that the enablement rejection is improper.

Finally, the Applicant disagrees with the Examiner's assertions as to lack of guidance and unpredictability. As discussed in detail in the previous response, no undue experimentation is necessary to practice the claimed invention. The instant specification teaches the properties, routes of administration, and dosages of the antibodies to be administered, and exemplifies the desired pharmacological effect. One of skill in the art would understand that a preferred dose achieves the maximal response, and would also be able to correlate dosages and desired responses by other means, such as measurement of EGFR-tyrosine kinase activity for determination of receptor saturation. Accordingly, an effective dose or dose intensity of an anti-EGFR antibody is either known to, or readily can be determined by, one of ordinary skill in the art. Dosage evaluations are routinely conducted as part of the development of a drug, for example in preclinical and clinical trials.

With regard to unpredictability, Applicant points out that what is claimed is a treatment for psoriasis, and not a treatment for cancer. The unpredictability presumed by the Examiner springs from an unsupported supposition that CPT-11 is essential for the psoriasis resolution that is observed in the working example.

In summary, the Applicant asserts that the scope of the pending claims is reasonably enabled by the specification and that no undue experimentation is necessary to practice the claimed invention. The Applicant respectfully requests that the rejection be withdrawn.

Second Rejection Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection of claim 48 under 35 U.S.C. 112, first paragraph. The Examiner asserts "the specification fails to provide enough information for one of ordinary skill in the art to produce a chimeric antibody with exactly the same characteristics as the C225 antibody, because the specification fails to provide the structure and specific sequence for the claimed C225 antibody." More specifically, the Examiner contends that "amino acid sequence of the framework regions and regions other than the CDR portion can affect the structural conformation of an antibody and determine its antigen binding properties," and that such sequence is not provided.

Applicant respectfully reminds the Examiner that C225 is a chimeric antibody with a murine variable region (heavy and light chain variable domains) and human constant region (heavy and light chain constant domains). The specification specifically refers to U.S. Patent Nos. 4,816,397 and 4, 816,567 for chimeric antibodies. (See, specification, p. 8, ll. 10-14). C225 is not a humanized antibody. Consequently, the CDRs and frameworks are native. With respect to the identity of C225, the specification also provides that preferred chimeric antibodies are derived from the murine antibody called 225 and described in U.S. Patent No. 4,943,533. (See, specification, p. 10, ll. 10-12). Further, Wels et al. (see, specification, p. 10, ll. 4-6) provides the amino acid sequence (CDRs and frameworks) of M225, and accordingly, C225.

Thus, the instant specification discloses all of the amino acid sequences that affect antibody confirmation and determine binding properties, and one of ordinary skill in the art

can practice the invention of Claim 48. Applicant respectfully requests that the rejection be withdrawn.

Conclusion

It is respectfully submitted that all claims in the present application are in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicant's representative to discuss any issue that would expedite allowance of the subject application.

Respectfully submitted,

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